General

Guideline Title

Ulcerative colitis. Management in adults, children and young people.

Bibliographic Source(s)

National Clinical Guideline Centre. Ulcerative colitis. Management in adults, children and young people. London (UK): National Institute for Health and Care Excellence (NICE); 2013 Jun. 37 p. (Clinical guideline; no. 166).

Guideline Status

This is the current release of the guideline.

Recommendations

Major Recommendations

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Clinical Guideline Centre (NCGC) on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

Note: The wording used in the recommendations in this guideline (for example, words such as 'offer' and 'consider') denotes the certainty with which the recommendation is made (the strength of the recommendations). See the end of the "Major Recommendations" field for further descriptions of the strength of recommendations.

Patient Information and Support

Discuss the disease and associated symptoms, treatment options, and monitoring:

- With the person with ulcerative colitis, and their family members or carers as appropriate and
- Within the multidisciplinary team (the composition of which should be appropriate for the age of the person) at every opportunity.

Apply the principles in Patient experience in adult National Health Service services (NICE clinical guideline 138).

Discuss the possible nature, frequency, and severity of side effects of drug treatment for ulcerative colitis with the person, and their family members, or carers as appropriate. Refer to the NICE guideline Medicines adherence. Involving patients in decisions about prescribed medicines and supporting adherence (NICE clinical guideline 76).

Give the person, and their family members or carers as appropriate, information about their risk of developing colorectal cancer and about colonoscopic surveillance, in line with:

- Colonoscopic surveillance for prevention of colorectal cancer in people with ulcerative colitis, Crohn's disease, or adenomas (NICE clinical guideline 118)
- Referral for suspected cancer (NICE clinical guideline 27)[1]

Inducing Remission in People with Ulcerative Colitis

Treating Mild to Moderate Ulcerative Colitis: Step 1 Therapy

Proctitis and Proctosigmoiditis

To induce remission in people with a mild to moderate first presentation or inflammatory exacerbation of proctitis or proctosigmoiditis:

- Offer a topical aminosalicylate[2] alone (suppository or enema, taking into account the person's preferences) or
- Consider adding an oral aminosalicylate[3] to a topical aminosalicylate or
- Consider an oral aminosalicylate[3] alone, taking into account the person's preferences and explaining that this is not as effective as a topical aminosalicylate alone or combined treatment.

To induce remission in people with a mild to moderate first presentation or inflammatory exacerbation of proctitis or proctosigmoiditis who cannot tolerate or who decline aminosalicylates, or in whom aminosalicylates are contraindicated:

- Offer a topical corticosteroid or
- Consider oral prednisolone[4], taking into account the person's preferences.

To induce remission in people with subacute proctitis or proctosigmoiditis, consider oral prednisolone[4], taking into account the person's preferences.

Left-sided and Extensive Ulcerative Colitis

To induce remission in adults with a mild to moderate first presentation or inflammatory exacerbation of left-sided or extensive ulcerative colitis:

- Offer a high induction dose of an oral aminosalicylate.
- Consider adding a topical aminosalicylate or oral beclometasone dipropionate[5], taking into account the person's preferences.

To induce remission in children and young people with a mild to moderate first presentation or inflammatory exacerbation of left-sided or extensive ulcerative colitis:

- Offer an oral aminosalicylate[3,6].
- Consider adding a topical aminosalicylate[2] or oral beclometasone dipropionate[7], taking into account the person's preferences (and those of their parents or carers as appropriate).

To induce remission in people with a mild to moderate first presentation or inflammatory exacerbation of left-sided or extensive ulcerative colitis who cannot tolerate or who decline aminosalicylates, in whom aminosalicylates are contraindicated or who have subacute ulcerative colitis, offer oral prednisolone[4].

Treating Mild to Moderate Ulcerative Colitis: Step 2 Therapy

All Extents of Disease

Consider adding oral prednisolone[4] to aminosalicylate therapy to induce remission in people with mild to moderate ulcerative colitis if there is no improvement within 4 weeks of starting step 1 aminosalicylate therapy or if symptoms worsen despite treatment. Stop beclometasone dipropionate if adding oral prednisolone.

Consider adding oral tacrolimus[8] to oral prednisolone to induce remission in people with mild to moderate ulcerative colitis if there is an inadequate response to oral prednisolone after 2 to 4 weeks.

For guidance on infliximab for treating subacute ulcerative colitis (all extents of disease), refer to the NICE guideline Infliximab for subacute manifestations of ulcerative colitis (NICE technology appraisal guidance 140).

Treating Acute Severe Ulcerative Colitis: All Extents of Disease

The Multidisciplinary Team

For people admitted to hospital with acute severe ulcerative colitis:

- Ensure that a gastroenterologist and a colorectal surgeon collaborate to provide treatment and management.
- Ensure that the composition of the multidisciplinary team is appropriate for the age of the person.
- Seek advice from a paediatrician with expertise in gastroenterology when treating a child or young person.
- Ensure that the obstetric and gynaecology team is included when treating a pregnant woman.

Step 1 Therapy

For people admitted to hospital with acute severe ulcerative colitis (either a first presentation or an inflammatory exacerbation):

- Offer intravenous corticosteroids to induce remission and
- Assess the likelihood that the person will need surgery (see "Assessing Likelihood of Needing Surgery," below).

Consider intravenous ciclosporin[9] or surgery for people:

- Who cannot tolerate or who decline intravenous corticosteroids or
- For whom treatment with intravenous corticosteroids is contraindicated.
  Take into account the person's preferences when choosing treatment.

Step 2 Therapy

Consider adding intravenous ciclosporin[9] to intravenous corticosteroids or consider surgery for people:

- Who have little or no improvement within 72 hours of starting intravenous corticosteroids or
- Whose symptoms worsen at any time despite corticosteroid treatment
  Take into account the person's preferences when choosing treatment.

For guidance on infliximab for treating acute severe ulcerative colitis (all extents of disease) in people for whom ciclosporin is contraindicated or clinically inappropriate, refer to the NICE guideline Infliximab for acute exacerbations of ulcerative colitis (NICE technology appraisal guidance 163).

Monitoring Treatment

Ensure that there are documented local safety monitoring policies and procedures (including audit) for adults, children, and young people receiving treatment that needs monitoring (aminosalicylates, tacrolimus, ciclosporin, infliximab, azathioprine, and mercaptopurine). Nominate a member of staff to act on abnormal results and communicate with general practitioners and people with ulcerative colitis (and/or their parents or carers as appropriate).

Assessing Likelihood of Needing Surgery

Assess and document on admission, and then daily, the likelihood of needing surgery for people admitted to hospital with acute severe ulcerative colitis.

Be aware that there may be an increased likelihood of needing surgery for people with any of the following:

- Stool frequency more than 8 per day
- Pyrexia
- Tachycardia
- An abdominal X-ray showing colonic dilatation
- Low albumin, low haemoglobin, high platelet count, or C-reactive protein (CRP) above 45 mg/litre (bear in mind that normal values may be different in pregnant women)

Information about Treatment Options for People Who Are Considering Surgery

These recommendations apply to anyone with ulcerative colitis considering elective surgery. The principles can also be applied to people requiring emergency surgery.

Information When Considering Surgery

For people with ulcerative colitis who are considering surgery, ensure that a specialist (such as a gastroenterologist or a nurse specialist) gives the person (and their family members or carers as appropriate) information about all available treatment options, and discusses this with them. Information should include the benefits and risks of the different treatments and the potential consequences of no treatment.

Ensure that the person (and their family members or carers as appropriate) has sufficient time and opportunities to think about the options and the implications of the different treatments.

Ensure that a colorectal surgeon gives any person who is considering surgery (and their family members or carers as appropriate) specific information about what they can expect in the short and long term after surgery, and discusses this with them.

Ensure that a specialist (such as a colorectal surgeon, a gastroenterologist, an inflammatory bowel disease nurse specialist, or a stoma nurse) gives any person who is considering surgery (and their family members or carers as appropriate) information about:

- Diet
- Sensitive topics such as sexual function
- Effects on lifestyle
- Psychological wellbeing
- The type of surgery, the possibility of needing a stoma and stoma care

Ensure that a specialist who is knowledgeable about stomas (such as a stoma nurse or a colorectal surgeon) gives any person who is having surgery (and their family members or carers as appropriate) specific information about the siting, care, and management of stomas.

Information after Surgery

After surgery, ensure that a specialist who is knowledgeable about stomas (such as a stoma nurse or a colorectal surgeon) gives the person (and their family members or carers as appropriate) information about managing the effects on bowel function. This should be specific to the type of surgery performed (ileostomy or ileoanal pouch) and could include the following:

- Strategies to deal with the impact on their physical, psychological, and social wellbeing
- Where to go for help if symptoms occur
- Sources of support and advice

Maintaining Remission in People with Ulcerative Colitis

Proctitis and Proctosigmoiditis

To maintain remission after a mild to moderate inflammatory exacerbation of proctitis or proctosigmoiditis, consider the following options, taking into account the person's preferences:

- A topical aminosalicylate[2] alone (daily or intermittent) or
- An oral aminosalicylate[3] plus a topical aminosalicylate[2] (daily or intermittent) or
- An oral aminosalicylate[3] alone, explaining that this may not be as effective as combined treatment or an intermittent topical aminosalicylate alone

Left-sided and Extensive Ulcerative Colitis

To maintain remission in adults after a mild to moderate inflammatory exacerbation of left-sided or extensive ulcerative colitis:

- Offer a low maintenance dose of an oral aminosalicylate.
- When deciding which oral aminosalicylate to use, take into account the person's preferences, side effects and cost.

To maintain remission in children and young people after a mild to moderate inflammatory exacerbation of left-sided or extensive ulcerative colitis:

- Offer an oral aminosalicylate[3,6] when deciding which oral aminosalicylate to use, take into account the person's preferences (and those of their parents or carers as appropriate), side effects, and cost.

All Extents of Disease

Consider oral azathioprine[10] or oral mercaptopurine[10] to maintain remission:

- After two or more inflammatory exacerbations in 12 months that require treatment with systemic corticosteroids or
- If remission is not maintained by aminosalicylates

To maintain remission after a single episode of acute severe ulcerative colitis:

- Consider oral azathioprine[10] or oral mercaptopurine[10].
- Consider oral aminosalicylates in people who cannot tolerate or who decline azathioprine and/or mercaptopurine, or in whom azathioprine and/or mercaptopurine are contraindicated.

Dosing Regimen for Oral Aminosalicylates

Consider a once-daily dosing regimen for oral aminosalicylates[11] when used for maintaining remission. Take into account the person's preferences, and explain that once-daily dosing can be more effective, but may result in more side effects.

Pregnant Women

When caring for a pregnant woman with ulcerative colitis:

- Ensure effective communication and information-sharing across specialties (for example, primary care, obstetrics and gynaecology, and gastroenterology).
- Give her information about the potential risks and benefits of medical treatment to induce or maintain remission and of no treatment, and discuss this with her. Include information relevant to a potential admission for an acute severe inflammatory exacerbation.

Monitoring

Monitoring Bone Health

Adults

For recommendations on assessing the risk of fragility fracture in adults, refer to the NGC summary of the NICE guideline Osteoporosis: assessing the risk of fragility fracture (NICE clinical guideline 146).

Children and Young People

Consider monitoring bone health in children and young people with ulcerative colitis in the following circumstances:

- During chronic active disease
- After treatment with systemic corticosteroids
- After recurrent active disease

Monitoring Growth and Pubertal Development in Children and Young People

Monitor the height and body weight of children and young people with ulcerative colitis against expected values on centile charts (and/or z scores) at the following intervals according to disease activity:

- Every 3 to 6 months:
  - If they have an inflammatory exacerbation and are approaching or undergoing puberty or
  - If there is chronic active disease or
  - If they are being treated with systemic corticosteroids
- Every 6 months during pubertal growth if the disease is inactive
- Every 12 months if none of the criteria above are met

Monitor pubertal development in young people with ulcerative colitis using the principles of Tanner staging, by asking screening questions and/or carrying out a formal examination.

Consider referral to a secondary care paediatrician for pubertal assessment and investigation of the underlying cause if a young person with ulcerative colitis:

- Has slow pubertal progress or
- Has not developed pubertal features appropriate for their age

Monitoring of growth and pubertal development:

- Can be done in a range of locations (for example, at routine appointments, acute admissions or urgent appointments in primary care, community services, or secondary care)
- Should be carried out by appropriately trained healthcare professionals as part of the overall clinical assessment (including disease activity) to help inform the need for timely investigation, referral and/or interventions, particularly during pubertal growth.
  If the young person prefers self-assessment for monitoring pubertal development, this should be facilitated where possible and they should be instructed on how to do this.

Ensure that relevant information about monitoring of growth and pubertal development and about disease activity is shared across services (for example, community, primary, secondary, and specialist services). Apply the principles in Patient experience in adult NHS services (NICE clinical guideline 138) in relation to continuity of care.

Footnotes

[1]This guideline is being updated (publication date to be confirmed).

[2]At the time of publication (June 2013), some topical aminosalicylates did not have a UK marketing authorisation for this indication in children and young people. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information.

[3]At the time of publication (June 2013), some oral aminosalicylates did not have a UK marketing authorisation for this indication in children and young people. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information.

[4]Refer to the British National Formulary for guidance on stopping oral prednisolone therapy.

[5]At the time of publication (June 2013), beclometasone dipropionate only has a UK marketing authorisation 'as add-on therapy to 5-aminosalicylic acid (5-ASA) containing drugs in patients who are non-responders to 5-ASA therapy in active phase'. For use outside these licensed indications, the prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information.

[6]Dosing requirements for children should be calculated by body weight, as described in the British National Formulary.

[7]At the time of publication (June 2013), beclometasone dipropionate did not have a UK marketing authorisation for this indication in children and young people. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information.

[8]At the time of publication (June 2013), tacrolimus did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information.

[9]At the time of publication (June 2013), ciclosporin did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information.

[10]Although use is common in UK clinical practice, at the time of publication (June 2013) azathioprine and mercaptopurine did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information.

[11]At the time of publication (June 2013), not all oral aminosalicylates had a UK marketing authorisation for once-daily dosing. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information.

Definitions:

Strength of Recommendations

Some recommendations can be made with more certainty than others. The Guideline Development Group (GDG) makes a recommendation based on the trade-off between the benefits and harms of an intervention, taking into account the quality of the underpinning evidence. For some interventions, the GDG is confident that, given the information it has looked at, most patients would choose the intervention. The wording used in the recommendations in this guideline denotes the certainty with which the recommendation is made (the strength of the recommendation).

Interventions That Must (or Must Not) Be Used

The GDG usually uses 'must' or 'must not' only if there is a legal duty to apply the recommendation. Occasionally 'must' (or 'must not') is used if the consequences of not following the recommendation could be extremely serious or potentially life threatening.

Interventions That Should (or Should Not) Be Used – a 'Strong' Recommendation

The GDG uses 'offer' (and similar words such as 'refer' or 'advise') when confident that, for the vast majority of patients, an intervention will do more good than harm, and be cost effective. Similar forms of words (for example, 'Do not offer…') are used when the GDG is confident that an intervention will not be of benefit for most patients.

Interventions That Could Be Used

The GDG uses 'consider' when confident that an intervention will do more good than harm for most patients, and be cost effective, but other options may be similarly cost effective. The choice of intervention, and whether or not to have the intervention at all, is more likely to depend on the patient's values and preferences than for a strong recommendation, and so the healthcare professional should spend more time considering and discussing the options with the patient.

Clinical Algorithm(s)

The full version of the original guideline document includes the following algorithms:

- Inducing remission in people with mild to moderate ulcerative colitis
- Inducing remission in people with acute severe ulcerative colitis (all extents of disease)

In addition, a NICE pathway titled "Ulcerative Colitis Overview" is available at the National Institute for Health and Care Excellence Web site .

Scope

Disease/Condition(s)

Ulcerative colitis

Guideline Category

Counseling

Evaluation

Management

Risk Assessment

Treatment

Clinical Specialty

Colon and Rectal Surgery

Family Practice

Gastroenterology

Internal Medicine

Obstetrics and Gynecology

Oncology

Pediatrics

Surgery

Intended Users

Advanced Practice Nurses

Allied Health Personnel

Health Care Providers

Hospitals

Nurses

Patients

Pharmacists

Physician Assistants

Physicians

Public Health Departments

Guideline Objective(s)

- To offer best practice advice on assisting people with ulcerative colitis
- To address variation, and to help healthcare professionals to provide consistent high-quality care

Target Population

Adults (18 years and older), young people (12 to 17 years), and children (11 years or younger) with a diagnosis of ulcerative colitis, including consideration of specific needs of:

- Children and young people (including transition between paediatric and young adult services and puberty)
- Pregnant women

Note: This guideline does not include management of people with indeterminate colitis.

Interventions and Practices Considered

1. Providing patients, families, and carers information and support concerning ulcerative colitis, the risk of developing colorectal cancer, and about colonoscopic surveillance
2. Inducing remission with stepped therapy (treatment varies according to disease severity and patient preference)
    - Topical aminosalicylate alone (suppository or enema)
    - Oral aminosalicylates
    - Topical corticosteroid
    - Oral prednisolone
    - Intravenous corticosteroids
    - Intravenous ciclosporin
    - Combination therapy
    - Infliximab
    - Consideration of surgery
3. Providing information concerning risks/benefits of surgery to patients and families before and after surgery (information provided by specialist)
4. Maintaining remission (treatment varies according to disease severity and patient preference)

    - Topical aminosalicylate alone
    - Oral aminosalicylates
    - Combination therapy
    - Oral azathioprine or oral mercaptopurine
5. Special considerations for pregnant women
6. Monitoring bone health
7. Monitoring growth and pubertal development in children and young people

Major Outcomes Considered

- Mortality
- Remission and relapse
- Health-related quality of life
- Growth in children
- Onset of puberty or pubertal development
- Adverse events, including effects on fertility
- Admissions to hospital (including length of stay)
- Surgery, specifically colectomy
- Quality-adjusted life year (QALY)
- Cost-effectiveness

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Searches of Unpublished Data

Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Clinical Guideline Centre (NCGC) on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

Developing the Review Questions and Outcomes

Review questions were developed in a PICO framework (patient, intervention, comparison, and outcome) for intervention reviews, using population, presence or absence of factors under investigation (for example prognostic factors), and outcomes for prognostic reviews.

This use of a framework guided the literature searching process, critical appraisal and synthesis of evidence, and facilitated the development of recommendations by the Guideline Development Group (GDG). The review questions were drafted by the NCGC technical team and refined and validated by the GDG. The GDG chose approximately 7 outcomes identifying which outcomes were critical to their decision making and which were important. This distinction helped the GDG to make judgements about the importance of the different outcomes and their impact on decision making. For example, mortality will usually be considered a critical outcome and would be given greater weight when considering the clinical effectiveness of an intervention than an important outcome with less serious consequences. The GDG decide on the relative importance in the review protocol before seeing the review. The questions were based on the key clinical issues identified in the scope (see Appendix A in the full version of the original guideline document).

A total of 8 review questions were identified (see Chapter 3 of the full version of the original guideline document). Full literature searches, critical

appraisals, and evidence reviews were completed for all the specified review questions.

Searching for Evidence

Clinical Literature Search

The aim of the literature search was to identify all available, relevant published evidence in relation to the key clinical questions generated by the GDG. Systematic literature searches were undertaken to identify evidence within the published literature in order to answer the review questions as per the Guidelines Manual (2009) (see the "Availability of Companion Documents" field). Clinical databases were searched using relevant medical subject headings, free-text terms and study type filters where appropriate. Studies published in languages other than English were not reviewed. Where possible, searches were restricted to articles published in the English language. All searches were conducted on core databases, MEDLINE, EMBASE, the Cumulative Index to Nursing and Allied Health Literature (CINAHL), and The Cochrane Library. All searches were updated on 15th November 2012. No papers published after this date were considered.

Search strategies were checked by looking at reference lists of relevant key papers, checking search strategies in other systematic reviews, and asking the GDG for known studies in a specific area. The questions, the study types applied, the databases searched, and the years covered can be found in Appendix D in the full version of the original guideline document.

During the scoping stage, a search was conducted for guidelines and reports on the websites listed below and on organisations relevant to the topic. Searching for grey literature or unpublished literature was not undertaken. All references sent by stakeholders were considered.

- Guidelines International Network database (www.g-i-n.net)
- National Guideline Clearinghouse (www.guideline.gov/)
- National Institute for Health and Care Excellence (NICE) (www.nice.org.uk)
- National Institutes of Health Consensus Development Program (consensus.nih.gov/)
- Health Information Resources, NHS Evidence (www.library.nhs.uk/)

The titles and abstracts of records retrieved by the searches were scanned for relevance to the GDG's review questions. Any potentially relevant publications were obtained in full text. These were assessed against the inclusion criteria and the reference lists were scanned for any articles not previously identified. Further references were also suggested by the GDG.

Call for Evidence

The GDG decided to initiate a 'call for evidence' for the 'what information is needed for people considering surgery' review question as they believed that important evidence existed that would not be identified by the standard searches. The NCGC contacted all registered stakeholders and asked them to submit any relevant published or unpublished evidence.

Health Economic Literature Search

Systematic literature searches were also undertaken to identify health economic evidence within the published literature relevant to the review questions. The evidence was identified by conducting a broad search relating to the guideline population in the National Health Service Economic Evaluation Database (NHS EED), the Health Economic Evaluations Database (HEED) and Health Technology Assessment (HTA) databases with no date restrictions. Additionally, the search was run on MEDLINE and EMBASE, with a specific economic filter, to ensure recent publications that had not yet been indexed by these databases were identified. Studies published in languages other than English were not reviewed. Where possible, searches were restricted to articles published in the English language. The search strategies for health economics are included in Appendix D in the full version of the original guideline. All searches were updated on 15th November 2012. No papers published after this date were considered.

Evidence of Effectiveness

The evidence was reviewed following the steps shown schematically in Figure 1 in the full version of the original guideline:

- Potentially relevant studies were identified for each review question from the relevant search results by reviewing titles and abstracts. Full papers were then obtained.
- Full papers were reviewed against pre-specified inclusion/exclusion criteria to identify studies that addressed the review question in the appropriate population (review protocols are included in Appendix C in the full version of the original guideline).

Inclusion/Exclusion

The inclusion/exclusion of studies was based on the review protocols (see Appendix C in the full version of the original guideline document). The

GDG were consulted about any uncertainty regarding inclusion/exclusion.

The guideline population was defined to be adults, children, and young people with ulcerative colitis. For some review questions, the review population was confined to special groups such as people who are either in remission or with active disease of varying severity or pregnant women.

Randomised trials, non-randomised trials, and observational studies (including prognostic studies) were included in the evidence reviews as appropriate. Laboratory studies (in vivo or in vitro) were excluded.

Conference abstracts were not automatically excluded from the review but were initially assessed against the inclusion criteria and then further processed only if no other full publication was available for that review question, in which case the authors of the selected abstracts were contacted for further information. Conference abstracts included in Cochrane reviews were included when they met the review inclusion criteria and authors were not contacted. Literature reviews, letters and editorials, foreign language publications, and unpublished studies were excluded.

The review protocols are presented in Appendix C in the full version of the original guideline document. Excluded studies (with their exclusion reasons) are listed in Appendix F in the full version of the original guideline document.

Type of Studies

For most intervention reviews in this guideline, parallel randomised controlled trials (RCTs) were included because they are considered the most robust type of study design that could produce an unbiased estimate of the intervention effects. Cross over RCTs were not appropriate for estimating the intervention effects for with the induction of remission of ulcerative colitis as their baseline severity of disease level was likely to have changed. Only data from the first intervention people were exposed to were included from randomised crossover studies in the review. For the prognostic review on the risk factors of poor bone health in children and young people, cross-sectional, prospective, and retrospective studies were included and for the prognostic review on predicting the outcome of acute severe ulcerative colitis, prospective and retrospective cohort studies were included. Case control studies were not included.

Evidence of Cost-effectiveness

The health economist:

- Identified potentially relevant studies for each review question from the economic search results by reviewing titles and abstracts – full papers were then obtained
- Reviewed full papers against pre-specified inclusion/exclusion criteria to identify relevant studies (see below for details)

Inclusion/Exclusion

Full economic evaluations (studies comparing costs and health consequences of alternative courses of action: cost–utility, cost–effectiveness, cost–benefit, and cost–consequence analyses) and comparative costing studies that addressed the review question in the relevant population were considered potentially applicable as economic evidence.

Studies that only reported cost per hospital (not per patient), or only reported average cost-effectiveness without disaggregated costs and effects, were excluded. Abstracts, posters, reviews, letters/editorials, foreign language publications, and unpublished studies were excluded. Studies judged to have an applicability rating of 'not applicable' were excluded (this included studies that took the perspective of a non-Organisation for Economic Co-operation and Development [OECD] country).

Remaining studies were prioritised for inclusion based on their relative applicability to the development of this guideline and the study limitations. For example, if a high quality, directly applicable UK analysis was available other less relevant studies may not have been included. Where exclusions occurred on this basis, this is noted in the relevant section.

For more details about the assessment of applicability and methodological quality see the economic evaluation checklist (the Guidelines Manual, Appendix F [see the "Availability of Companion Documents" field) and the health economics research protocol in Appendix C in the full version of the original guideline document.

When no relevant economic analysis was found from the economic literature review, relevant UK National Health Service unit costs related to the compared interventions were considered by the GDG to inform the possible economic implication of the recommendation they wished to make.

Number of Source Documents

The number of studies identified for each clinical question is provided in Appendix E in the full version of the original guideline document (see the

"Availability of Companion Documents" field).

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Overall Quality of Outcome Evidence in Grading of Recommendations Assessment, Development and Evaluation (GRADE)

Level	Description
High (++++)	Further research is very unlikely to change confidence in the estimate of effect.
Moderate (+++O)	Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate.
Low (++OO)	Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate.
Very Low (+OOO)	Any estimate of effect is very uncertain.

Methods Used to Analyze the Evidence

Meta-Analysis

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Clinical Guideline Centre (NCGC) on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

Evidence of Effectiveness

The evidence was reviewed following the steps shown schematically in Figure 1 in the full version of the original guideline document:

- Relevant studies were critically appraised using the appropriate checklists as specified in the Guidelines Manual (see the "Availability of Companion Documents" field). For prognostic studies, quality was assessed using the checklist for Prognostic studies (NICE Guidelines Manual, 2009).
- Key information was extracted on the study's methods and patient, intervention, comparison and outcome (PICO) factors and results were presented in evidence tables (see Appendix G in the full version of the original guideline document).
- Summaries of the evidence were generated by outcome (included in the relevant chapter write-ups) and were presented in Guideline Development Group (GDG) meetings:
    - Randomised studies: meta-analysed, where appropriate, and reported in Grading of Recommendations Assessment, Development and Evaluation (GRADE) profiles
    - Prognostic studies: assessing risk factors; data were presented as a range of values, usually in terms of the relative effect as reported by the authors and where possible reported in the GRADE profile format.
    - Prognostic studies evaluating risk tools were presented as measures of prognostic test accuracy (sensitivity, specificity, positive and negative predictive value). Coupled values of sensitivity and specificity were summarised in Receiver Operating Curves (ROC) to allow visual comparison between different index tests (plotting data at different thresholds) and to investigate heterogeneity more effectively (given data were reported at the same thresholds). A meta-analysis could not be conducted because the studies reported

data at various thresholds.

Twenty percent (20%) of each of the above stages of the reviewing process was quality assured by the second reviewer to eliminate any potential of reviewer bias or error.

Methods of Combining Clinical Studies

Data Synthesis for Intervention Reviews

Where possible, meta-analyses were conducted to combine the results of studies for each review question using Cochrane Review Manager (RevMan5) software. Where studies reported data which could not be analysed by meta-analysis a narrative summary is provided.

Fixed-effects (Mantel-Haenszel) techniques were used to calculate pooled risk ratios (relative risk) for binary outcomes. For continuous outcomes, measures of central tendency (mean) and variation (standard deviation [SD]) were required for meta-analysis. Data for continuous outcomes were analysed using an inverse variance method for pooling mean differences, and where the studies had different scales, standardised mean differences were used. A generic inverse variance option in Review Manager was used if any studies reported solely the summary statistics and 95% confidence interval (CI) (or standard error) – this included any hazard ratios reported. However, in cases where standard deviations were not reported per intervention group, the standard error (SE) for the mean difference was calculated from other reported statistics - p-values or 95% CI; meta-analysis was then undertaken for the mean difference and standard error using the generic inverse variance method in Cochrane Review Manager (RevMan5) software. Stratified analyses were predefined for some review questions at the protocol stage when the GDG identified that these strata are different in terms of biological and clinical characteristics and the interventions were expected to have a different effect on these groups of people with ulcerative colitis. For example, stratifying by frequency of relapses and current use of immunomodulators prior to the trial.

Statistical heterogeneity was assessed by visually examining the forest plots, and by considering the chi-squared test for significance at $p<0.1$ and the I-squared inconsistency statistic (with an I-squared value of more than 50% indicating considerable heterogeneity). Where considerable heterogeneity was present, the NCGC technical team carried out sensitivity analyses. Sensitivity analyses were carried out looking at the subgroups which were pre-specified by the GDG. If the heterogeneity still remained, a random effects (DerSimonian and Laird) model was employed to provide a more conservative estimate of the effect.

For interpretation of the binary outcome results, differences in the absolute event rate were calculated using the GRADEpro software, for the median event rate across the control arms of the individual studies in the meta-analysis. The hazard ratio can be translated into an absolute difference in the proportion of patients who are event-free at a particular time point, assuming proportional hazards. This is calculated using GRADEpro software. Absolute risk differences were presented in the GRADE profiles and in a clinical summary of findings tables, for discussion with the GDG.

Network meta-analyses (NMAs) were conducted for the review questions in adults on the induction of remission of mild or moderate left-sided or extensive ulcerative colitis and the maintenance of remission after a mild or moderate inflammatory exacerbation of left-sided or extensive ulcerative colitis. This type of analysis simultaneously compared multiple treatments in a single meta-analysis, preserving the randomization of randomised controlled trials (RCTs) included in the reviews of direct comparisons. The aim of the NMAs were to include all relevant evidence in order to answer questions on the clinical effectiveness of interventions when no direct comparison was available and to give a ranking of treatments in terms of efficacy.

A hierarchical Bayesian NMA was performed using the software WinBUGS version 1.4. The NCGC technical team used statistical models for fixed and random effects that allowed inclusion of multi-arm trials and accounts for the correlation between arms in the trials with any number of trial arms. The model was based on original work from the University of Bristol (https://www.bris.ac.uk/cobm/research/mpes/mtc.html). The quality of each NMA was assessed using the NICE checklist, "NICE DSU evidence synthesis of treatment efficacy in decision making: a reviewer's checklist."

Heterogeneity was assessed in the results of the random effects model by using the method described by Dias et al. which compares the size of the treatment effect to the extent of between trials variation.

Inconsistency in the networks was tested by comparing any available direct and indirect treatment comparison and testing the null hypothesis that the indirect evidence was not different than the direct evidence on the relative risk ratio scale using the normal distribution; inconsistency was identified if the median estimates (median relative risk ratios) of the direct comparisons were outside the confidence intervals of the relative risk ratios as generated from the NMA output.

There were three main outputs from the NMA: 1) the estimation of log odds and relative risk ratios (ORs and RRs) (with their 95% credible intervals) were calculated for comparisons of the direct and indirect evidence, 2) the probability that each treatment was best based on the proportion of Markov chain iterations in which treatment had the highest probability of achieving the outcomes selected in the networks and 3) the

ranking of treatments compared to placebo groups (presented as median rank and its 95% credible intervals).

Data Synthesis for Prognostic Factor Reviews

Risk Factors for Poor Bone Health in Children and Young People with Ulcerative Colitis

ORs, RRs, or hazard ratios (HRs), with their 95% CIs for the effect of the pre-specified prognostic factors were extracted from the papers. Studies of lower risk of bias were preferred, taking into account the analysis and the study design; in particular, prospective cohort studies that reported multivariable analyses, which included key confounders as identified by the GDG at the protocol stage for that outcome.

The results from the risk factors of poor bone health in children and young people was presented as a narrative due to the lack of published data.

Risk Tools for Predicting the Outcome of Acute Severe Ulcerative Colitis

Coupled forest plots of sensitivity and specificity with their 95% CIs across studies (at various thresholds) were produced for each risk tool, using Cochrane Review Manager (RevMan5) software. In order to do that, 2 by 2 tables (the number of true positives, false positives, true negatives, and false negatives) were either directly taken from the study if given or derived from raw data, or were calculated from the set of test accuracy statistics.

To allow comparison between tests, summary ROC curves were generated for each prognostic test from the pairs of sensitivity and specificity calculated from the 2 x 2 tables, selecting one threshold per study. An ROC plot shows true positive rate (i.e., sensitivity) as a function of false positive rate (i.e., 1 – specificity). Data were entered into Review Manager 5 software and ROC curves were fitted using the Moses Littenburg approach.

Area under the ROC curve (AUC) data for each study was also plotted on a graph, for each prognostic test: the AUC describes the overall prognostic accuracy across the full range of thresholds. The GDG agreed on the following criteria for AUC: <=0.50 worse than chance; 0.50-0.60 = very poor; 0.61-0.70 = poor; 0.71-0.80 = moderate; 0.81-0.92 = good; 0.91-1.00 = excellent or perfect test. Heterogeneity or inconsistency amongst studies was visually inspected in the forest plots, if appropriate (only when there were similar thresholds). A prognostic meta-analysis was not conducted mainly because of the different thresholds across studies and the complexity of the analysis and time and resource constraints of this guideline development.

Type of Analysis

Estimates of effect from individual studies were based on the author reported data. As a preference available case analysis (ACA) was used and if this was not reported intention to treat analysis (ITT) was then used.

The available case analysis method is preferred to an intention-to-treat with imputation analysis (ITT), in order to avoid making assumptions about the participants for whom outcome data were not available, and furthermore assuming that those with missing outcome data have the same event rate as those who continue. In addition, ITT analysis tends to bias the results towards no difference, and therefore the effect may be smaller than in reality.

Appraising the Quality of Evidence by Outcomes

The evidence for outcomes from the included RCTs and observational studies (when appropriate) was evaluated and presented using the 'GRADE toolbox' developed by the international GRADE working group (http://www.gradeworkinggroup.org/). The software (GRADEpro) developed by the GRADE working group was used to assess the evidence quality for each outcome, taking into account individual study quality factors and the meta-analysis results. Results were presented in GRADE profiles ('GRADE tables'), which consist of two adjacent sections: the "Clinical/Economic Study Characteristics" table includes details of the quality assessment while the "Clinical /Economic Summary of Findings" table includes pooled outcome data and an absolute measure of the intervention effect and the summary of quality of evidence for that outcome. In this table, the columns for intervention and control indicate summary measures and measures of dispersion (such as mean and standard deviation or median and range) for continuous outcomes and frequency of events (n/N: the sum across studies of the number of patients with events divided by sum of the number of completers) for binary outcomes.

The evidence for each outcome was examined separately for the quality elements listed and defined in Table 1 in the full version of the original guideline document and each graded using the quality levels listed in Table 2 in the full version of the original guideline document. The main criteria considered in the rating of these elements are discussed below. Footnotes were used to describe reasons for grading a quality element as having serious or very serious problems. The ratings for each component were summed to obtain an overall assessment for each outcome.

Grading the Quality of Clinical Evidence

After results were pooled, the overall quality of evidence for each outcome was considered. The following procedure was adopted when using GRADE:

1. A quality rating was assigned, based on the study design. RCTs start HIGH and observational studies as LOW, uncontrolled case series as LOW.
2. The rating was then downgraded for the specified criteria: Risk of bias (study limitations), inconsistency, indirectness, imprecision, and publication bias. These criteria are detailed in section 3.3 of the full version of the original guideline document. Evidence from observational studies (that had not previously been downgraded) was upgraded if there was: a large magnitude of effect, dose-response gradient, and if all plausible confounding would reduce a demonstrated effect or suggest a spurious effect when results showed no effect. Each quality element considered to have "serious" or "very serious" risk of bias was rated at 1 or 2 points respectively.
3. The downgraded/upgraded marks were then summed and the overall quality rating was revised. For example, all RCTs started as HIGH and the overall quality became MODERATE, LOW, or VERY LOW if 1, 2, or 3 points were deducted respectively.
4. The reasons used for downgrading were specified in the footnotes.

The details of criteria used for each of the main quality elements are discussed further in Sections 3.3.5 to 3.3.8 in the full version of the original guideline document.

Evidence of Cost-effectiveness

Literature Review

The health economist:

- Critically appraised relevant studies using the economic evaluations checklist as specified in the Guidelines Manual (see the "Availability of Companion Documents" field).
- Extracted key information about the study's methods and results into evidence tables (evidence tables are included in Appendix G in the full version of the original guideline document).
- Generated summaries of the evidence in NICE economic evidence profiles (included in the relevant chapter write-ups in the full version of the original guideline document).

NICE Economic Evidence Profiles

The NICE economic evidence profile has been used to summarise cost and cost-effectiveness estimates. The economic evidence profile shows, for each economic study, an assessment of applicability and methodological quality, with footnotes indicating the reasons for the assessment. These assessments were made by the health economist using the economic evaluation checklist from the Guidelines Manual, Appendix H (see the "Availability of Companion Documents" field). It also shows incremental costs, incremental outcomes (for example, quality-adjusted life-years [QALYs]) and the incremental cost-effectiveness ratio from the primary analysis, as well as information about the assessment of uncertainty in the analysis.

If a non-UK study was included in the profile, the results were converted into pounds sterling using the appropriate purchasing power parity.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Clinical Guideline Centre (NCGC) on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

This guidance was developed in accordance with the methods outlined in the NICE Guidelines Manual 2009 (see the "Availability of Companion Documents" field).

A multidisciplinary Guideline Development Group (GDG) comprising professional group members and consumer representatives of the main stakeholders developed this guideline. The group met every six weeks during the development of the guideline.

Developing Recommendations

Over the course of the guideline development process, the GDG was presented with:

- Evidence tables of the clinical and economic evidence reviewed from the literature. All evidence tables are in Appendix G of the full version of the original guideline document.
- Summary of clinical (Grading of Recommendations Assessment, Development, and Evaluation [GRADE] tables) and economic evidence and quality (as presented in Chapters 5-9 of the full version of the original guideline document; see the "Availability of Companion Documents" field).
- Forest plots and Receiver Operating Curves (ROC) (see Appendix H in the full version of the original guideline document).
- A description of the methods and results of the cost-effectiveness analysis undertaken for the guideline (see Appendix L in the full version of the original guideline document).

Recommendations were drafted on the basis of the GDG's interpretation of the available evidence, taking into account the trade off between benefits, harms, and costs of different courses of action. This was either done formally in an economic model, or informally. Firstly, the net benefit over harm was considered (clinical effectiveness), using the critical outcomes. When this was done informally, the GDG took into account the clinical benefits/harms when one intervention was compared with another. The assessment of net benefit was moderated by the importance placed on the outcomes (the GDG's values and preferences), and the confidence the GDG had in the evidence (evidence quality). Secondly, it was assessed whether the net benefit justified the costs. Results of the Network meta-analyses was also taken into account in the drafting of recommendations and were incorporated in the health economic modelling for considering the most clinical and cost-effective treatment.

When clinical and economic evidence was of poor quality, conflicting, or absent, the GDG drafted recommendations based on their expert opinion. The considerations for making consensus based recommendations included the balance between potential harms and benefits, economic or other implications compared to the benefits, current practices, recommendations made in other relevant guidelines, patient preferences, and equality issues. The consensus recommendations were done through discussions in the GDG. The GDG could also consider whether the uncertainty is sufficient to justify delaying making a recommendation to await further research, taking into account the potential harm of failing to make a clear recommendation. The wording of recommendations was agreed by the GDG and focused on the following factors:

- On the actions health professionals need to take
- Include what readers need to know
- Reflect the strength of the recommendation (for example the word 'offer' was used for strong recommendations and 'consider' for weak recommendations)
- Emphasise the involvement of the patient (and/or their carers if needed) in decisions on treatment and care
- Follow NICE's standard advice on recommendations about drugs, waiting times, and ineffective interventions

The main considerations specific to each recommendation are outlined in the 'Recommendations and link to evidence' sections within each chapter of the full version of the original guideline document.

Rating Scheme for the Strength of the Recommendations

Strength of Recommendations

Some recommendations can be made with more certainty than others. The Guideline Development Group (GDG) makes a recommendation based on the trade-off between the benefits and harms of an intervention, taking into account the quality of the underpinning evidence. For some interventions, the GDG is confident that, given the information it has looked at, most patients would choose the intervention. The wording used in the recommendations in this guideline denotes the certainty with which the recommendation is made (the strength of the recommendation).

Interventions That Must (or Must Not) Be Used

The GDG usually uses 'must' or 'must not' only if there is a legal duty to apply the recommendation. Occasionally 'must' (or 'must not') is used if the consequences of not following the recommendation could be extremely serious or potentially life threatening.

Interventions That Should (or Should Not) Be Used – a 'Strong' Recommendation

The GDG uses 'offer' (and similar words such as 'refer' or 'advise') when confident that, for the vast majority of patients, an intervention will do more good than harm, and be cost effective. Similar forms of words (for example, 'Do not offer…') are used when the GDG is confident that an intervention will not be of benefit for most patients.

Interventions That Could Be Used

The GDG uses 'consider' when confident that an intervention will do more good than harm for most patients, and be cost effective, but other options may be similarly cost effective. The choice of intervention, and whether or not to have the intervention at all, is more likely to depend on the patient's values and preferences than for a strong recommendation, and so the healthcare professional should spend more time considering and discussing the options with the patient.

Cost Analysis

Undertaking New Health Economic Analysis

As well as reviewing the published economic literature for each review question new economic analysis was undertaken by the health economist in priority areas. Priority areas for new health economic analysis were agreed by the Guideline Development Group (GDG) after formation of the review questions and consideration of the available health economic evidence.

Additional data for the analysis was identified as required through additional literature searches undertaken by the health economist, and discussion with the GDG. Model structure, inputs and assumptions were explained to and agreed by the GDG members during meetings, and they commented on subsequent revisions.

Cost-effectiveness Criteria

In general, an intervention was considered to be cost-effective if either of the following criteria applied (given that the estimate was considered plausible):

a. The intervention dominated other relevant strategies (that is, it was both less costly in terms of resource use and more clinically effective compared with all the other relevant alternative strategies), or
b. The intervention cost less than £20,000 per quality-adjusted life-year (QALY) gained compared with the next best strategy.

If the GDG recommended an intervention that was estimated to cost more than £20,000 per QALY gained, or did not recommend one that was estimated to cost less than £20,000 per QALY gained, the reasons for this decision are discussed explicitly in the 'from evidence to recommendations' section of the relevant chapter with reference to issues regarding the plausibility of the estimate or to the factors set out in the National Institute for Health and Care Excellence (NICE) report 'Social value judgements: principles for the development of NICE guidance'.

If a study reported the cost per life year gained but not QALYs, the cost per QALY gained was estimated by multiplying by an appropriate utility estimate to aid interpretation. The estimated cost per QALY gained is reported in the economic evidence profile with a footnote detailing the life-years gained and the utility value used. When QALYs or life years gained are not used in the analysis, results are difficult to interpret unless one strategy dominates the others with respect to every relevant health outcome and cost.

See the individual chapters of the full version of the original guideline document (see the "Availability of Companion Documents" field) for discussions of the cost-effectiveness of specific recommendations.

Original Cost-Effectiveness Analysis

The original cost-effectiveness analysis conducted for this guideline suggests that low dose oral aminosalicylate (ASA) is the most cost-effective option to maintain remission in patients with left sided or extensive ulcerative colitis, although there is considerable uncertainty related to interpretation of the withdrawals data.

See Appendix L in the full version of the original guideline document (see the "Availability of Companion Documents" field) for health economic analysis/analyses undertaken for the guideline.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

The guidance is subject to a six week public consultation and feedback as part of the quality assurance and peer review the document. All comments received from registered stakeholders are responded to in turn and posted on the National Institute for Health and Care Excellence (NICE) website when the pre-publication check of the full guideline occurs.

The final draft was submitted to the Guideline Review Panel for review prior to publication.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendations is not specifically stated.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate management of ulcerative colitis

See the "Trade off between clinical benefits and harms" sections of the full version of the original guideline document for additional details about benefits of specific interventions.

Potential Harms

- Adverse effects of oral, topical, or intravenous drugs
- The Guideline Development Group (GDG) noted that nephrotoxicity and opportunistic infections may be an issue with longer term use of tacrolimus and recommended regular monitoring. Nephrotoxicity (increase by >30% of baseline creatinine level) occurred in 14.8% of participants followed up at 12 weeks (2 week trial followed by a 10 week open label extension). Monitoring for toxicity including renal dysfunction, low magnesium, and infection was considered essential by the GDG.
- The GDG discussed the needs of people with acute severe ulcerative colitis and the importance of balancing the risks of continued medical treatment with surgery. This focused on the adverse events associated with intravenous steroids and, in particular, immunosuppression associated with ciclosporin.
- In one study, when 5-aminosalicylic acid (5-ASA) was used in combination with immunomodulators, there was an associated higher rate of premature birth.
- The GDG recognised that there are harms associated with a high false positive rate (unnecessarily identifying someone as needing surgery) with use of a prognostic risk tool. Secondary therapy would be initiated earlier and there would be higher surgical rates, resulting in higher costs, adverse events, and lower quality of life. There are also harms associated with a high false negative rate (not identifying someone who needs surgery). Secondary therapy may be started too late. As a result, there may be a higher surgery rate potentially leading to higher financial costs, adverse events, and lower quality of life; and a greater risk of surgical complications as the patients may be sicker and a higher risk of mortality.
- There could be a risk that monitoring growth too frequently could pick up 'false delay in growth' and treatment could be changed unnecessarily resulting in changes to treatment that are premature.

See the "Trade off between clinical benefits and harms" sections of the full version of the original guideline document for additional details about harms of specific interventions.

Qualifying Statements

Qualifying Statements

- This guidance represents the view of the National Institute for Health and Care Excellence (NICE), which was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer, and informed by the summaries of product characteristics of any drugs.
- Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity and foster good relations. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties.
- Treatment and care should take into account individual needs and preferences. Patients should have the opportunity to make informed decisions about their care and treatment, in partnership with their healthcare professionals. If the patient is under 16, their family or carers should also be given information and support to help the child or young person to make decisions about their treatment. Healthcare professionals should follow the Department of Health's advice on consent . If someone does not have capacity to make decisions, healthcare professionals should follow the code of practice that accompanies the Mental Capacity Act and the supplementary code of practice on deprivation of liberty safeguards. In Wales, healthcare professionals should follow advice on consent from the Welsh Government.
- If a young person is moving between paediatric and adult services, care should be planned and managed according to the best practice guidance described in the Department of Health's Transition: getting it right for young people. Adult and paediatric healthcare teams should work jointly to provide assessment and services to young people with ulcerative colitis. Diagnosis and management should be reviewed throughout the transition process, and there should be clarity about who is the lead clinician to ensure continuity of care.
- For all recommendations, NICE expects that there is discussion with the patient about the risks and benefits of the interventions, and their values and preferences. This discussion aims to help them to reach a fully informed decision.
- The guideline will assume that prescribers will use a drug's summary of product characteristics to inform decisions made with individual patients.
- This guideline recommends some drugs for indications for which they do not have a UK marketing authorisation at the date of publication, if there is good evidence to support that use. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. The patient (or those with authority to give consent on their behalf) should provide informed consent, which should be documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information. Where recommendations have been made for the use of drugs outside their licensed indications ('off-label use'), these drugs are marked with a footnote in the recommendations.

Implementation of the Guideline

Description of Implementation Strategy

The National Institute for Health and Care Excellence (NICE) has developed tools to help organisations implement this guidance. These are available on the NICE Web site (see also the "Availability of Companion Documents" field).

Key Priorities for Implementation

The following recommendations have been identified as priorities for implementation.

Patient Information and Support

- Discuss the disease and associated symptoms, treatment options, and monitoring:
  - With the person with ulcerative colitis, and their family members or carers as appropriate and
  - Within the multidisciplinary team (the composition of which should be appropriate for the age of the person) at every opportunity

Apply the principles in the NICE clinical guideline Patient experience in adult National Health Service services (NICE clinical guideline 138).

Inducing Remission: Step 1 Therapy for Mild to Moderate Ulcerative Colitis

- To induce remission in people with a mild to moderate first presentation or inflammatory exacerbation of proctitis or proctosigmoiditis:

    - Offer a topical aminosalicylate[1] alone (suppository or enema, taking into account the person's preferences) or
    - Consider adding an oral aminosalicylate[2] to a topical aminosalicylate or
    - Consider an oral aminosalicylate[2] alone, taking into account the person's preferences and explaining that this is not as effective as a topical aminosalicylate alone or combined treatment.
- To induce remission in adults with a mild to moderate first presentation or inflammatory exacerbation of left-sided or extensive ulcerative colitis:
    - Offer a high induction dose of an oral aminosalicylate.
    - Consider adding a topical aminosalicylate or oral beclomethasone dipropionate[3], taking into account the person's preferences.
- To induce remission in children and young people with a mild to moderate first presentation or inflammatory exacerbation of left-sided or extensive ulcerative colitis:
    - Offer an oral aminosalicylate[2,4].
    - Consider adding a topical aminosalicylate[1] or oral beclometasone dipropionate[5], taking into account the person's preferences (and those of their parents or carers as appropriate).

Inducing Remission: Step 2 Therapy for Acute Severe Ulcerative Colitis

- Consider adding intravenous ciclosporin[6] to intravenous corticosteroids or consider surgery for people:
    - Who have little or no improvement within 72 hours of starting intravenous corticosteroids or
    - Whose symptoms worsen at any time despite corticosteroid treatment

Take into account the person's preferences when choosing treatment.

Monitoring Treatment

- Ensure that there are documented local safety monitoring policies and procedures (including audit) for adults, children, and young people receiving treatment that needs monitoring (aminosalicylates, tacrolimus, ciclosporin, infliximab, azathioprine, and mercaptopurine). Nominate a member of staff to act on abnormal results and communicate with general practitioners (GPs) and people with ulcerative colitis (and/or their parents or carers as appropriate).

Assessing Likelihood of Needing Surgery

- Assess and document on admission, and then daily, the likelihood of needing surgery for people admitted to hospital with acute severe ulcerative colitis.

Information about Treatment Options for People Who Are Considering Surgery

- For people with ulcerative colitis who are considering surgery, ensure that a specialist (such as a gastroenterologist or a nurse specialist) gives the person (and their family members or carers as appropriate) information about all available treatment options, and discusses this with them. Information should include the benefits and risks of the different treatments and the potential consequences of no treatment.
- After surgery, ensure that a specialist who is knowledgeable about stomas (such as a stoma nurse or a colorectal surgeon) gives the person (and their family members or carers as appropriate) information about managing the effects on bowel function. This should be specific to the type of surgery performed (ileostomy or ileoanal pouch) and could include the following:
    - Strategies to deal with the impact on their physical, psychological, and social wellbeing
    - Where to go for help if symptoms occur
    - Sources of support and advice

Maintaining Remission

- Consider a once-daily dosing regimen for oral aminosalicylates[7] when used for maintaining remission. Take into account the person's preferences, and explain that once-daily dosing can be more effective, but may result in more side effects.

Footnotes

[1]At the time of publication (June 2013), some topical aminosalicylates did not have a UK marketing authorisation for this indication in children and young people. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information.

[2]At the time of publication (June 2013), some oral aminosalicylates did not have a UK marketing authorisation for this indication in children and young people. The prescriber should

follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information.

[3]At the time of publication (June 2013), beclometasone dipropionate only has a UK marketing authorisation 'as add-on therapy to 5-aminosalicylic acid (5-ASA) containing drugs in patients who are non-responders to 5-ASA therapy in active phase'. For use outside these licensed indications, the prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information.

[4]Dosing requirements for children should be calculated by body weight, as described in the British National Formulary.

[5]At the time of publication (June 2013), beclometasone dipropionate did not have a UK marketing authorisation for this indication in children and young people. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information.

[6]At the time of publication (June 2013), ciclosporin did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information.

[7]At the time of publication (June 2013), not all oral aminosalicylates had a UK marketing authorisation for once-daily dosing. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information.

Implementation Tools

Audit Criteria/Indicators

Clinical Algorithm

Foreign Language Translations

Mobile Device Resources

Patient Resources

Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

National Clinical Guideline Centre. Ulcerative colitis. Management in adults, children and young people. London (UK): National Institute for Health and Care Excellence (NICE); 2013 Jun. 37 p. (Clinical guideline; no. 166).

Adaptation

Not applicable: The guideline was not adapted from another source.

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Guideline Developer(s)

National Guideline Centre - National Government Agency [Non-U.S.]

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National Institute for Health and Care Excellence (NICE)

Guideline Committee

Guideline Development Group (GDG)

Composition of Group That Authored the Guideline

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Financial Disclosures/Conflicts of Interest

At the start of the guideline development process all Guideline Development Group (GDG) members declared interests including consultancies, fee-paid work, share-holdings, fellowships, and support from the healthcare industry. At all subsequent GDG meetings, members declared arising conflicts of interest, which were also recorded (see Appendix B in the full version of the original guideline document [see the "Availability of Companion Documents" field]).

Members were either required to withdraw completely or for part of the discussion if their declared interest made it appropriate. The details of declared interests and the actions taken are shown in Appendix B of the full version of the original guideline document.

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available from the National Institute for Health and Care Excellence (NICE) Web site . Also available for download as a Kindle or EPUB ebook from the NICE Web site .

Availability of Companion Documents

The following are available:

- Ulcerative colitis. Management in adults, children and young people. Full guideline. London (UK): National Institute for Health and Care Excellence (NICE); 2013 Jun. 297 p. (Clinical guideline; no 166). Electronic copies: Available in Portable Document Format (PDF) from the National Institute for Health and Care (NICE) Web site .
- Ulcerative colitis. Management in adults, children and young people. Appendices. London (UK): National Institute for Health and Care Excellence (NICE); 2013 Jun. 134 p. (Clinical guideline; no 166). Electronic copies: Available in PDF from the NICE Web site .
- Ulcerative colitis. Management in adults, children and young people. Baseline assessment tool. London (UK): National Institute for Health and Care Excellence (NICE); 2013 Jun. (Clinical guideline; no 166). Electronic copies: Available from the NICE Web site .
- Ulcerative colitis. Management in adults, children and young people. Clinical audit tools. London (UK): National Institute for Health and Care Excellence (NICE); 2013 Jun. (Clinical guideline; no 166). Electronic copies: Available from the NICE Web site .
- Ulcerative colitis. Management in adults, children and young people. Costing report. London (UK): National Institute for Health and Care Excellence (NICE); 2013 Jun. 30 p. (Clinical guideline; no 166). Electronic copies: Available in PDF from the NICE Web site .
- Ulcerative colitis. Management in adults, children and young people. Costing template. London (UK): National Institute for Health and Care Excellence (NICE); 2013 Jun. (Clinical guideline; no 166). Electronic copies: Available from the NICE Web site .
- Ulcerative colitis. NICE pathway. London (UK): National Institute for Health and Care Excellence (NICE). Electronic copies: Available from the NICE Web site .
- The guidelines manual 2009. London (UK): National Institute for Health and Care Excellence (NICE); 2009 Jan. Electronic copies: Available in PDF from the NICE Archive Web site .

Patient Resources

The following is available:

- Ulcerative colitis. Information for the public. London (UK): National Institute for Health and Care Excellence (NICE); 2013 Jun. Electronic copies: Available from the National Institute for Health and Care Excellence (NICE) Web site . Also available for download as a Kindle or EPUB ebook from the NICE Web site . Also available in Welsh from the NICE Web site .

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